REMARKS

Claims 1-43 are now pending in this application. Claims 1-9, 14-29 and 34-43 are rejected. Claims 10-13 and 30-33 are objected to for being dependent upon rejected base claims. Claims 2, 3, 26 to 29, 39 and 40 are cancelled herein. New claims 44-50 are added herein.

The limitation of original claim 3 is incorporated into claim 1 as amended. The limitation of original claim 40 has been incorporated into claim 38. Claim 4 has been amended so that it depends on claim 14. In addition, claims 5, 6, 7, 9, 14, 17, 22, 23, 30, 32, 34, 35 and 41 have been amended. The basis for new claims 44 to 47 can be found in the specification on page 19. The basis for new claim 48 comes from original claim 32. The basis for claims 49 and 50 can be found in the specification on page 20.

Claims 14-25 and 34-35 are rejected under 35 U.S.C. §112, second paragraph, as being indefinite. Claim 14 has been amended to replace "simulated transport function" with "tissue transport function" to resolve the indefiniteness issue for claims 14-25. Claim 34 has been amended to define F and claim 35 has been amended to depend from claim 34 to resolve the indefiniteness issue for claims 34-35.

Claims 1-6, 26-29 and 36-43 are rejected under 35 U.S.C. §102(e) as being anticipated by Ostergaard (U.S. Pat. No. 7,069,068).

MPEP §2131 states that "[a] claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference." *citing Verdegaal Bros. v. Union Oil Co. of California*, 814 F.2d 628, 631, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987). The MPEP elaborates further by saying that "[t]he elements must be arranged as required by the claim."

In order to address the rejections, claims 2, 26 to 29 and 39 have been cancelled and original claims 3 and 40 have been incorporated into independent claims 1 and 38, respectively. Applicant respectfully traverses the rejections and, alternatively, avers that the claims as amended overcome the rejections.

In regard to claim 1, the Office Action asserts that equations 11 and 12 in column 15 of Ostergaard discloses how to derive parameters (equation 12) and calculate blood perfusion indices (CBF in equation 12) using a transport function (equation 11 in Ostergaard). However, claim 1 includes the features of: (1) deriving parameters from the contrast agent concentration data using at least one

transport function that accounts for delay and dispersion of the contrast agent; (2) wherein the at least one transportation function includes an arterial transport function $h_a(t)$ represented by a first model through a vessel leading to the region of interest (ROI); and (3) calculating the perfusion indices from the derived parameters. In contrast, the method described by Ostergaard, with regard to equations 11 and 12, is known as singular value decomposition (SVD) deconvolution method.

The SVD deconvolution method, which has also been summarized in the "background to the invention" section of the present application (page 1, lines 16 to 28), does not account for arterial delay and dispersion effects of the contrast agent as required by claim 1 of the present application. Equation 11 does not use a transport function, but instead describes a convolution between the arterial input function $C_a(t)$ with the vascular residue function R(t). Moreover, the SVD deconvolution method described in Ostergaard's patent describes a model-free approach that assumes the input function to the tissue ROI is already known. In practice, however, it is difficult to measure the arterial input function at the input to different tissues of interest. This is due to the practicalities that arteries directly feeding the tissues are usually small in size and subject to a substantial partial voluming effect. Therefore, it is practically useful to select an input function from a normal large artery further upstream from

the region of interest. This may be reasonable in normal situations, however, in the case of major vessel disease, such as acute stroke or carotid artery stenosis, the AIF selected from a major artery is often associated with a delay and dispersion before it reaches the abnormal tissue of interest. Thus, the SVD deconvolution method described in Ostergaard's patent is unable to distinguish arterial delay and dispersion from prolonged tissue MTT and hence impairs its clinical application.

Furthermore, in the present invention, as recited in the claims and illustrated in Fig. 3 of the current application, an arterial transport function is represented by a first model through a vessel leading up to the region of interest 6. This arterial vessel is designated as 62. Thus, measurements are conducted by selecting the arterial input function further upstream from the region of interest and not at the entry point to the region of interest 60. In other words, it is not possible to measure the input function at the entry point to the ROI at point 60. Therefore, an AIF is selected further upstream in the major artery 62, and then, using a model taking into account the delay and dispersion effects associated with the contrast agent moving from 62 to 60, a figure is arrived at for the arterial input function at the entry point 60. In contrast, Ostergaard makes an assumption as to what the AIF is at the entry point to the ROI. This is then used to obtain information about blood flow and other parameters through the tissue or ROI.

Moreover, the numerical process of solving the equations and deriving perfusion parameters in the current application, in line with feature 3 of claim 1 mentioned above, is different from that disclosed in the Ostergaard patent. The present application uses algorithms that are based on non-linear systems. In contrast, Ostergaard uses algorithms based on linear algebra.

As previously mentioned, claim 1 now incorporates the feature of original claim 3, while claim 38 incorporates the feature of original claim 40. In other words, claims 1 and 40 as amended incorporate a first model used to represent an arterial *transport* function through a vessel leading to the ROI. Ostergaard does not disclose a first model used to represent an arterial *transport* function through a vessel leading to the ROI. The Office Action asserts that example 3 of "Ostergaard exemplifies modeling cerebral blood flow with the required arterial transport function listed in equations 21-22 in column 29 of Ostergaard ." Office Action page 5. However, such a feature is not disclosed in Ostergaard. The equations 21-22, referred to in the Office Action, describe how to convert the residue function into a probability density function that relates to the distribution of vascular paths of capillaries in normal brain tissue. However, Ostergaard's method (equations 21 and 22 in column 29) involves deconvolution of the arterial *input* function, which is completely different than the arterial *transport* function recited in the claims that describes blood transportation through arteries. Moreover, the probability density function of Ostergaard does not

account for contrast delay and dispersion effects in major blood vessels including arteries. Ostergaard, in example 3 and with particular reference to column 32, lines 35 to 53, only discusses a vascular model. Thus, there is no disclosure of an arterial transport function that accounts for delay and dispersion as is claimed in the present invention.

In light of the above discussion, it is clear that the cited reference does not includes all the features of the present invention as claimed. More specifically, Ostergaard does not disclose at least the features of: (1) deriving parameters from the contrast agent concentration data using at least one transport function that accounts for delay and dispersion of the contrast agent; (2) wherein the at least one transportation function includes an arterial transport function $h_a(t)$ represented by a first model through a vessel leading to the region of interest (ROI); and (3) calculating the perfusion indices from the derived parameters. Thus the claims, in particular 1 and 38, are not anticipated by Ostergaard.

In regard to claims 4 and 41, the cited art does not disclose a tissue transportation function that accounts for contrast delay and dispersion effects in arteries leading up to a region of interest. The Office Action asserts that example 5 of Ostergaard discloses "modeling renal plasma flow with the required tissue

transport function listed in equations 27 to 29 in column 45 Ostergaard." Office Action page 5. However, equations 27 to 29 describe how to convert the residue function into a transport function of a contrast agent in a kidney. Such a tissue transportation function does not account for contrast delay and dispersion effects in arteries leading up to the region of interest. In contrast, claim 4 recites using a second model to represent a tissue transport function through the region of interest which accounts for delay and dispersion of the contrast agent. Thus, claims 4 and 41 are not anticipated by the cited art because Ostergaard does not account for contrast delay and dispersion effects in arteries leading up to the region of interest.

In regard to claim 5, the cited art does not disclose selecting an arterial input function in the vessel leading up to the ROI. The Office Action asserts that "Ostergaard details the use of the AIF and pixels taken from the contrasting agent data." Office Action page 6. However, Ostergaard does not account for arterial delay and dispersion effects including the selection of an AIF in the vessel leading to the ROI. Thus, claim 5 is not anticipated by the cited art because, in contrast to Ostergaard, the pixels taken are of the contrast agent concentration data in the vessel leading up to the ROI.

In regard to claim 6, the cited art does not disclose measuring the contrast agent concentration remaining in the ROI particularly with the features recited in claims 1 and 5. Thus, the cited art does not disclose all the elements as recited in in claim 6.

Please note that the discussion above regarding claims 1 to 6 similarly applies to claim 38 -43.

Claims 7-9 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ostergaard in view of Folger (Elements of Chemical Engineering, 2nd Ed., 1992, chapter 13, section 13.4, pages 729-737). More specifically, the Office Action states that Ostergaard teaches all the elements recited in the claims except for the gamma variate function, which is disclosed in Folger. In other words, the rejection characterizes the structure recited in the claims as simply the combining of prior art elements according to known methods to yield predictable results.

MPEP §2141.01(a) states that "a reference in a field different from that of applicant's endeavor may be reasonably pertinent if it is one which, because of the matter with which it deals, logically would have commended itself to an inventor's attention in considering his or her invention as a whole." In addition, MPEP

§2143 states that when rejecting a claim based on the rationale that the recited structure is simply "combining prior art elements according to known methods to yield predictable results" there must be a "finding that the prior art included each element." *Id.* Moreover, for such a rejection it must be that one of "ordinary skill in the art would have recognized that the results of the combination were predictable." *Id.* In addition, there must be a finding that "each element merely performs the same function as it does separately." *Id.*

The prior art cited in the Office Action does not logically commend itself to combination, fails to include each element as recited in the claims, the results of the combination are not predictable and the elements in the cited art do not perform the same function when combined. Thus, applicant respectfully traverses the rejections and alternatively, avers that the claims as amended overcome the rejections.

The Office Action asserts that Fogler discloses "residence time distributions in reactors and step tracer analysis." Office Action page 10. From the examples in Fogler's text, numerical solutions are used to describe the tracer concentrations for realistic complex reactor systems. However, the solutions are based upon known structures with known physical parameters. In contrast, the vascular structure in a living biological system is unknown.

The aim of the perfusion measurements in the present invention is to derive information about the unknown vascular system by measuring the input and the output or residue, which is essentially a reverse problem solving technique in contrast to chemical reactors. The present invention seeks to obtain blood perfusion indices in a region of interest that includes deriving parameters from a contrast agent concentration data using at least one transport function that accounts for delay and dispersion of the contrast agent. One of those transport functions is the arterial transport function that is represented by a first model through a vessel that leads up to the region of interest. This is not disclosed, for the aforementioned reasons, in the Ostergaard patent.

Furthermore, Fogler relates to chemical reactor systems and tracer analysis thereof. It would not have been obvious or, in fact, a matter of routine for a person skilled in the art to combine the disclosure of Fogler with that of Ostergaard to make claims 7 to 9 obvious. Fogler is not in a similar field of technology as it discloses concepts about chemical reactor systems modeled on known structures with known physical parameters. As the present invention is concerned about perfusion measurement about an unknown vascular system, one skilled in the art would not be lead to read and understand what is disclosed in the Fogler document, and then combine that knowledge with information in the Ostergaard patent to

arrive at all of the features in claims 7 to 9. Moreover, neither Ostergaard nor Fogler disclose the gamma variate function in present claim 7.

Therefore, claims 7 to 9 are not rendered obvious by Ostergaard in view of Folger. Folger does not commend itself to combination with Ostergaard, because Folger addresses systems with known structures. Furthermore, the cited references even in combination fail to include each element as recited in the claims as neither discloses the gamma variate function recited in the claims. Moreover, the results of the combination are not predictable and the elements in the cited art do not perform the same function when combined because Folger is addressing concepts about chemical reactor systems modeled on known structures as opposed to unknown structures.

In light of the foregoing, the application is now believed to be in proper form for allowance of all claims and notice to that effect is earnestly solicited.

In this amendment, there are twenty four (24) claims in excess of twenty. Applicant has previously paid for twenty three (23) claims in excess of twenty. Thus, applicant is required to pay for one (1) additional claim. Accordingly, the fee of $50 for the one (1) additional claim is provided for in the charge

authorization presented in the PTO Form 2038, Credit Card Payment form, provided herewith.

Respectfully submitted,

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